



US007820681B1

(12) **United States Patent**  
**Davis**

(10) **Patent No.:** **US 7,820,681 B1**  
(45) **Date of Patent:** **Oct. 26, 2010**

(54) **METHODS FOR CONCOMITANT  
ADMINISTRATION OF COLCHICINE AND A  
SECOND ACTIVE AGENT**

(75) Inventor: **Matthew W. Davis**, Erwinna, PA (US)

(73) Assignee: **Mutual Pharmaceutical Company,  
Inc.**, Philadelphia, PA (US)

(\*) Notice: Subject to any disclaimer, the term of this  
patent is extended or adjusted under 35  
U.S.C. 154(b) by 0 days.

(21) Appl. No.: **12/372,046**

(22) Filed: **Feb. 17, 2009**

#### Related U.S. Application Data

(60) Provisional application No. 61/152,067, filed on Feb.  
12, 2009, provisional application No. 61/138,141,  
filed on Jan. 14, 2009.

(51) **Int. Cl.**  
**A61K 31/167** (2006.01)  
**C07C 233/23** (2006.01)  
**C07C 211/41** (2006.01)

(52) **U.S. Cl.** ..... **514/263.31**; 564/123; 564/308;  
564/427; 568/306; 514/629

(58) **Field of Classification Search** ..... None  
See application file for complete search history.

#### (56) **References Cited**

##### U.S. PATENT DOCUMENTS

5,426,224	A *	6/1995	Lee et al.	564/177
5,914,332	A *	6/1999	Sham et al.	514/274
6,037,157	A	3/2000	Norbeck et al.	
6,896,900	B2 *	5/2005	Gosselin et al.	424/451
7,601,758	B1	10/2009	Davis	
7,619,004	B1	11/2009	Davis	

##### OTHER PUBLICATIONS

Leikin et al. Poisoning and toxicology handbook. Aug. 2007, p. 216.\*  
Herewege et al. A dual chamber model of female cervical mucosa for  
the study of HIV transmission and for the evaluation of candidate  
HIV microbicides. Antiviral Research, 74, 2007, 111-124.\*  
Creighton et al. Is ritonavir boosting associated with gout? Interna-  
tional journal of STD & AIDS, 2005, 16: 362-364.\*  
Vision Pharma (Colchicine Tablets USP, 0.6 mg, 2006).\*  
Leikin et al. Poisoning and toxicology handbook. Aug. 2007, pp.  
216-217.\*  
Temesgen et al. Tipranavir: a new option for the treatment of drug-  
resistant HIV infection. Reviews of Anti-infective agents. Sep. 15,  
2007.\*

Wang et al. 2001. HMG-CoA reductase inhibitors (statins) charac-  
terized as direct inhibition of P-glycoprotein. Pharmaceutical  
research, vol. 18, No. 6, pp. 800-806.\*

Drugs.Com; "Colchicine and Ritonavir Interactions"; printed Jan. 5,  
2009; "colchicine", printed Jan. 9, 2009; and "ritonavir", printed Jan.  
9, 2009.

Horn, et al.; "Life-Threatening Colchicine Drug Interactions"; Phar-  
macy Times; p. 111; (May 2006).

Hsu, et al.; "Ritonavir: Clinical Pharmacokinetics and Interactions  
with Other Anti-HIV Agents"; Clinical Pharmacokinetics; 35; pp. 275-  
291; (1998).

Niel, et al.; "Colchicine Today"; Joint Bone Spine; 73; pp. 672-678;  
(2006).

Perez-Ruiz, et al.; "Optimisation of the Treatment of Acute Gout";  
BioDrugs; 13; pp. 415-423; (2000).

Terkeltaub, Robert A.; "Gout"; The New England Journal of Medi-  
cine; 349; pp. 1647-1655; (2003).

Van Der Velden, et al.; "Colchicine-Induced Neuromyopathy in a  
Patient with Chronic Renal Failure: The Role of Clarithromycin";  
Netherlands Journal of Medicine; 66; pp. 204-206; (2008).

Zhou, et al.; "Clinical Outcomes and Management of Mechanism-  
Based Inhibition of Cytochrome P450 3A4"; Therapeutics and Clini-  
cal Risk Management; I; pp. 3-13; (2005).

Terkeltaub, et al.; "Comparison of Low-Dose vs High-Dose Oral  
Colchicine Regimens in Patients with Gout Flares"; Presentation at  
the American College of Rheumatology Scientific Meeting in San  
Francisco, CA; 23 pages; Oct. 24-29 (2008).

Terkeltaub, et al.; "The Clinical Relevance of P-gp and CYP 3A4 on  
Colchicine Metabolism and Elimination: Dosing Recommendations  
for Macrolide Antibiotics, Cyclosporine, Ketoconazole, Ritonavir  
and Diltiazem"; Presentation at the American College of Rheumatol-  
ogy Scientific Meeting in San Francisco, CA; 19 pages; Oct. 24-29  
(2008).

Krishnan et al.; "Gout in Ambulatory Care Settings in the United  
States"; Journal of Rheumatology; 35; pp. 498-501; (2008).

Lacy et al. Lexi-Comp's Clinical Reference Library, Drug Informa-  
tion Handbook, 7th Edition, 1999-2000), pp. 108-109 and 292-293.

\* cited by examiner

*Primary Examiner*—Brandon J Fetterolf

*Assistant Examiner*—Anna Pagonakis

(74) *Attorney, Agent, or Firm*—Cantor Colburn LLP

(57)

#### **ABSTRACT**

Methods for concomitant administration of colchicine  
together with one or more second active agents, e.g., keto-  
conazole and ritonavir, are disclosed. Such methods reduce  
the dangers commonly associated with such concomitant  
administration and provide additional benefits. Methods of  
notifying health care practitioners and patients regarding  
appropriate dosing for concomitant administration of colchi-  
cine together with second active agents are also provided.

**4 Claims, 5 Drawing Sheets**